

Introduction of *Haemophilus influenzae* type b vaccine into immunization programmes

Management guidelines, including
information for health workers and parents



**DEPARTMENT OF VACCINES
AND BIOLOGICALS**



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Glossary

The following terms, when used in this document, are defined as below.

Combination vaccine	A vaccine made by combining two or more other vaccines (for example, measles/mumps/rubella (MMR) is a combination vaccine).
Conjugate vaccine	A vaccine made by chemically joining two different substances; in the case of Hib vaccines, joining a protein with a polysaccharide.
Diluent	A liquid used to reconstitute a freeze-dried vaccine.
Formulation	The form in which a vaccine is presented (for example, liquid or lyophilized, single or in combination).
Lyophilized	Freeze-dried. Dried in a frozen state under high vacuum for preservation.
Monovalent vaccine	A vaccine containing antigen to induce protection against a single microorganism (for example, tetanus toxoid).

Acronyms

AEFI	adverse events following immunization
BCG	bacille Calmette-Guérin (vaccine)
DTaP	diphtheria–tetanus–acellular pertussis vaccine
DTP	diphtheria–tetanus–pertussis vaccine
FIC	fully immunized child
HepB	hepatitis B vaccine
Hib	<i>Haemophilus influenzae</i> type b
IPV	injectable polio vaccine
OPV	oral polio vaccine
TT	tetanus toxoid

1. Introduction

Infections due to *Haemophilus influenzae* are a major cause of morbidity and mortality in young children throughout the world. Six serotypes (types a-f) are known to cause disease, but type b is responsible for over 90% of the life-threatening *Haemophilus influenzae* infections in children, including meningitis and pneumonia. From 300 000 to 500 000 children die each year due to these *Haemophilus influenzae* type b (Hib) diseases.

Researchers have developed the new “conjugate” vaccines by connecting certain proteins with part of the Hib bacterium. The proteins enhance the immune response to the Hib component, and the vaccines protect children from the age of two months on.

Current Hib vaccine is safe and highly effective – 90-99% of children develop antibodies after three doses. It prevents meningitis, pneumonia, epiglottitis, and other serious infections caused by the Hib bacterium. In the United States, Hib cases declined 99% from 1986 to 1995 in children under five, as a result of the use of Hib vaccine.

WHO recommends that Hib vaccine now be included in routine infant immunization programmes for all children, as appropriate to national capacities and priorities. This manual provides managers with the information they need to implement a national decision to introduce Hib vaccine.

2. The epidemiology of Hib

2.1 The Hib bacterium

Haemophilus influenzae type b is one of six types (a, b, c, d, e, and f) of encapsulated strains of the bacteria. All six types are characterized by the following:

- They live in the nose and throat of people and usually do not cause serious illness.
- When they do cause serious illness, they mostly affect children under five years of age, they may become systemic, i.e. spread by the blood throughout the body, and can be life threatening.

Type b bacteria account for over 90% of serious *Haemophilus influenzae* infections in children.

2.2 The Hib diseases

Bacterial meningitis – Inflammation of the membranes that cover and protect the spinal cord and brain. Bacterial meningitis in children is usually caused by Hib. In industrialized countries, between 3% and 5% of these cases are fatal and in developing countries, as many as 40% result in death. Fifteen to 35% of children who survive Hib meningitis are left with permanent neurological disabilities such as mental retardation and hearing loss.

Pneumonia – Inflammation of the lungs. In developing countries, Hib is a major cause of pneumonia (or acute lower respiratory infection, ALRI) in children. One study in Africa showed that 20% of the bacterial pneumonia cases severe enough to be seen on chest X-ray were caused by Hib.

Other Hib infections include:

- *Epiglottitis* – Inflammation of the larynx and pharynx. In the absence of appropriate and immediate treatment, 50% of cases are fatal.
- *Septicaemia* – Presence of pathogenic bacteria in the blood.
- *Septic arthritis* – Inflammation of the joints.
- *Osteomyelitis* – Inflammation of the bones.

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- *Cellulitis* – Inflammation of tissue under the skin.
 - *Pericarditis* – Inflammation of the membrane around the heart.

2.3 Mode of transmission

Hib bacteria are passed from child to child in droplets of saliva expelled when an infected child coughs or sneezes. Hib also spreads when children share toys and other things that they have put in their mouths. Transmission is increased when many children spend prolonged periods of time together in settings such as day-care or creches.

2.4 Age distribution

Hib disease is most common in children under five years old, and children between the ages of four months and 12 months are most at risk.

At birth, maternal antibodies are adequate to protect most infants. Between two and three months of age, the level of these antibodies falls, and incidence of Hib infections increases. By four to five years of age, children develop their own immunity; thereafter, Hib disease occurs rarely.

3. Hib vaccine

3.1 Formulations

Several Hib conjugate vaccines are available from different manufacturers. All manufacturers use the capsular polysaccharide material of the bacteria and link it to tetanus toxoid, diphtheria toxoid, a diphtheria toxoid-like protein, or a mix of proteins from another bacterium. Each of these has been proven effective in the prevention of Hib disease.

New Hib vaccines are produced every year. The formulations available as of February 2000 include:

- Liquid Hib vaccine (monovalent)
- Liquid Hib and DTP vaccines in combination
- Liquid Hib and Hepatitis B (HepB) vaccines in combination
- Lyophilized (i.e. freeze-dried) Hib vaccine that the user mixes with saline diluent (monovalent)
- Lyophilized Hib vaccine that the user mixes with liquid DTP, DTP/HepB, DTP/IPV, DTaP, or DTaP/IPV in combination

All of these vaccines protect against *Haemophilus influenzae* type b but do not prevent diseases caused by other types of *Haemophilus influenzae*, such as bronchitis, otitis, and sinusitis. They do not prevent meningitis and pneumonia caused by other agents.

3.2 Interchangeability

Types and formulations of Hib vaccines can be interchanged, so vaccines from different manufacturers can be used for each dose that a child receives.

Diluents, both in saline form and made from other vaccines, are produced to go with specific Hib vaccines and **are not** interchangeable.

3.3 Presentation

Hib vaccine comes in 10-dose and single-dose glass vials and in single-dose pre-filled syringes. A new two dose formulation (a combination vaccine to be mixed with DTP/hepatitis B) will be available in 2001).

3.4 Storage volume

The storage volume of Hib vaccine in 10 dose vials (liquid or lyophilized) is approximately the same as for hepatitis B vaccine in 10 dose vials. The table below shows storage volumes of available, or soon to be available Hib vaccines and combinations.

Vaccine	Presentation	Packed volume per dose (cm ³ /dose)
Hib	liquid, single dose vial	32
	liquid, ten dose vial	9.5-13.8
	lyophilized, single dose vial	9.7
Hib/DTP	liquid, single dose vial	32
	liquid, 10 dose vial	13.8
	lyophilized, single dose vial with AD syringe	154.0
	lyophilized, 10 dose vial	11.9
Hib/DTP/HepB	lyophilized, two dose vial	9.7
	lyophilized, 10 dose vial	5.3

See the Product Information Sheets available from WHO headquarters for more information and for formulae to assess storage volume.

3.5 Storage temperature

Hib vaccine should be stored between 2° and 8°C. Liquid Hib vaccine must never be frozen. Lyophilized vaccine may be frozen until reconstitution, but since the most commonly used diluent, DTP, cannot be frozen, it is recommended to also store lyophilized Hib at 2-8°C, to avoid errors.

3.6 Shelf life

The shelf life of Hib vaccines is two years from the date of manufacture if stored between 2° and 8°C.

3.7 Price of vaccine

Like other new vaccines, Hib vaccine is more expensive than the traditional EPI vaccines. Nevertheless, the price of the vaccine has been decreasing for several years and continues to decline: for example in 2000, monovalent Hib vaccine could be purchased for between US\$ 2.00 and US\$ 3.00 per dose.

Since prices are changing and prices differ between countries, managers should check with their national procurement officers or with UNICEF or WHO before buying.

3.8 Indications

Hib vaccine is indicated in children from the age of 6 weeks up to 18 months.

3.9 Contra-indications

There are no contra-indications to Hib immunization, except a history of hypersensitivity to any of the components in the vaccine (for example, tetanus or diphtheria toxoids).

3.10 Schedule

Hib immunization schedules differ from country to country depending on the type of Hib vaccine used and the schedule for other vaccines.

In general, the scheduling practices below are followed:

- The first dose is given to children at six weeks of age or older.
- Three doses are given. Most Hib vaccines require three doses, and in the remainder of this document, a three-dose primary series will be considered routine. One conjugate is licensed for a two-dose primary series, but is not marketed widely.
- The interval between doses is not less than one month.
- The vaccine may be given at the same time as DTP, OPV, and (if applicable) HepB vaccines, as shown, for example, in the schedule below.

Age	Vaccines
6 weeks	DTP1, OPV1, HepB1, Hib1
10 weeks	DTP2, OPV2, HepB2, Hib2
14 weeks	DTP3, OPV3, HepB3, Hib3

3.11 Dosage

The size of a dose is 0.5 ml.

3.12 Administration

Liquid vaccine is used directly from the vial. Freeze-dried vaccine must be reconstituted before administration either with diluent or with another vaccine specifically identified and indicated for this purpose by the manufacturer, such as DTP.

Hib vaccine is given by intramuscular injection in the anterolateral aspect of the thigh (infants) or deltoid muscle (older children).

It can be given at the same time as DTP, OPV, IPV, and HepB vaccines without ill effect. However, if used as a monovalent vaccine, it should not be injected in the same limb at the same time as other vaccines.

3.13 Side effects

Hib vaccine has not been associated with any serious side effects. However, redness, swelling, and pain where the injection was given may occur in about 25% of children receiving the vaccine. These usually start within one day after the immunization and last from one to three days. Less commonly, children may develop fever or irritability for a short time after immunization. When given at the same time as DTP, the rate of fever and/or irritability is no higher than when DTP is given alone.

4. Management decisions

The introduction of Hib vaccine into a routine immunization programme, like the introduction of any new vaccine, requires management decision-making. Issues relating specifically to Hib vaccine are discussed below.

4.1 Which type of Hib vaccine is most suitable?

Hib vaccine is available in liquid and lyophilized formulations. Both liquid and lyophilized vaccines are available in combination with other vaccines, including but not limited to DTP and HepB. In deciding which formulation and combination to use, consider the following:

Liquid monovalent Hib – Use of the liquid monovalent formulation means that no reconstitution is required and that opened, multi-dose vials can be used in subsequent sessions, reducing vaccine wastage. However, the use of monovalent Hib vaccine will add another injection to the number a child receives already, and additional cold chain space is needed. A country in which ample cold chain space is available and in which preservation of local DTP production is a priority may select this option.

Liquid combination Hib (i.e. Hib and DTP) – Because this is a liquid vaccine, no reconstitution is required and the multi-dose vial policy applies. As a combination, it provides two vaccines in one injection and requires less cold chain space than would two monovalent vaccine formulations. For many developing countries, this may be the most attractive option. This option may not disrupt local DTP production, if compatibility of the locally produced DTP with Hib vaccine is demonstrated, and appropriate collaborative arrangements can be made for manufacturing.

Lyophilized monovalent (with saline diluent) – Use of this formulation preserves the potential for local DTP production but, because it is a monovalent vaccine, it requires an additional injection and storage space for the vaccine plus diluent (although diluent does not need refrigeration at most health care levels). It also requires a reconstitution step and equipment, increasing complexity and risk of contamination through human error. Finally, lyophilized vaccines to be diluted with diluent which does not contain preservative should not be used in sessions following the one in which they were reconstituted, thus, there is a greater potential for wastage with this formulation.

Lyophilized combination (i.e. Hib and DTP; Hib, DTP and HepB; other pentavalent products) – These combination vaccines reduce the number of injections from two to one and in the case of Hib, DTP and Hep B, from three injections to one. Local DTP production can be preserved, after compatibility of the DTP diluent is confirmed.

The lyophilized vaccines require reconstitution with its attendant complexity and risk of contamination. Countries may select this option especially if a reduced number of injections is highly valued.

4.2 How does Hib vaccine fit into the current immunization schedule?

Giving several immunizations at the same time simplifies planning for both parents and health workers and reduces costs. The closest match for Hib vaccine is the schedule for DTP and, in many countries, OPV and HepB as well. Immunizing a child with more than one of these antigens on the same day does not affect the efficacy of any of the antigens so administered.

In scheduling same-day immunizations, health workers should be prepared to deal with parents who are not happy with giving their children as many as three injections at the same time (i.e. DTP, HepB, and Hib).

4.3 Who should be immunized with Hib vaccine?

In the routine programme. All children should receive three doses of Hib vaccine in their first year, beginning after six weeks of age.

During Hib vaccine introduction. When Hib immunization is introduced, managers must decide whether to immunize only children born after the date of introduction (the gradual introduction strategy) or to include children born before that date as well (the catch-up strategy). Because of its simplicity and lower number of doses, most countries now introducing Hib vaccine use the gradual introduction strategy.

Gradual introduction strategy. Limiting immunizations to children born after Hib vaccine introduction has the following implications compared to using the catch-up strategy:

- There will be one three-dose schedule, not several schedules.
- Because fewer children will be immunized and the schedule is less complicated, the training needs for health workers, vaccines, and supplies will be less.
- Children born before the date of introduction will not be protected against Hib disease until their natural immunity becomes effective.
- There will be a slower decrease in cases.
- Parents may be reluctant to deny Hib immunization to children who are only a bit older than their immunized brothers and sisters.

Catch-up strategy. Including older children in the target population has the following implications:

- There will be multiple schedules in the first year for health workers and parents. For example, a schedule for catch-up dosing is outlined below:

For younger children:	
From 2 through 6 months of age	Full schedule of 3 doses

For older children:	
From 7 through 11 months of age	2 doses
From 12 through 18 months of age	1 dose

- Because more children will be immunized, the need for health workers, vaccines, and supplies will be increased.
- The decrease of cases during the first two years after Hib vaccine introduction will be more rapid.
- For older children who have already received DTP immunizations, monovalent Hib vaccine will have to be used, not a combination vaccine such as Hib-DTP, thus resulting in two Hib vaccine formations at the health centre level.

4.4 Should boosters be given?

In most countries, the primary series of Hib immunizations protect children through their most susceptible period and thus, in general, a booster is not needed. Although boosters may be considered when Hib disease is a substantial problem for children older than 12 months, some countries do not use booster doses even under these circumstances because of the increased cost and administrative complexity.

4.5 The multi-dose vial policy

The WHO multi-dose vial policy states that vials of liquid DTP, TT, HepB and OPV opened in a fixed clinic may be used at more than one immunization session provided that:

- a) The expiry date has not passed.
- b) The vaccines are stored under appropriate cold chain conditions.
- c) The vaccine vial septum has not been submerged in water.
- d) Aseptic technique has been used to withdraw all doses.
- e) The vaccine vial monitor (VVM), if attached, has not reached the discard point.

Reconstituted lyophilized vaccines such as BCG, measles and yellow fever must be discarded after six hours or at the end of a session, whichever comes first.

The WHO guidelines apply to Hib vaccines as follows:

- All liquid formulations of Hib vaccine contain a preservative and can be used in subsequent immunization sessions.
- The freeze-dried formulation (lyophilized) contains no preservatives, and after being reconstituted with a diluent with no preservatives, must be discarded at the end of the session or within six hours, whichever comes first (the same as for BCG, measles, and yellow fever).

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- Certain formulations of lyophilized Hib vaccine are supplied with DTP (or DTP/HepB) liquid vaccine or diluent containing preservatives. These reconstituted vaccines can be used safely over an extended period. However, the application of the multidose vial policy with DTP-HepB+Hib vaccine is recommended only if specific supervision and training activities are conducted in order to ensure appropriate implementation.

5. Operations

To introduce Hib vaccine into a routine immunization programme, systems need to be set up or adapted for ordering, storage, monitoring, and other activities. This section provides suggestions on how to manage these changes.

5.1 Ordering vaccine

As with other vaccines, allowance must be made in ordering for wastage or emergencies, such as transport delays or stock disruptions.

5.2 Storing vaccine and diluent

An assessment of storage requirements for Hib vaccines should be a part of the planning process. The following issues should be taken into consideration:

- Hib vaccines come in single-dose and multi-dose formats, either of which may be used to meet a country's needs.
Single-dose vials may be needed during catch-up activities and for reducing wastage, but the cost per dose of these vials is higher and they take up more volume than multi-dose vials.
- If a catch-up strategy is used (see Section 4) it will initially require single-dose vials of monovalent Hib for children who have had DTP immunizations.
- **Liquid Hib vaccine must never be frozen.**
- The volume of required storage space is not the same at each level. This is because diluents are often kept out of the cold chain at the central and regional levels. They are then refrigerated at the local level before being used to reconstitute the cold vaccine.
- The quadrivalent and pentavalent DTP+Hib and DTP-HepB+Hib formulations with lyophilized Hib are supplied in two separate vials (liquid DTP-HepB and lyophilized Hib) that are not packaged together. Lyophilized Hib vaccine can be stored either frozen at -20°C or refrigerated between 2°C and 8°C; however, liquid DTP or DTP-HepB vaccine **MUST NOT BE FROZEN**. To ensure that Hib is correctly reconstituted with DTP-HepB it is recommended that both vials of the pentavalent DTP-HepB+Hib formulation are stored together between 2°C and 8°C, and both vials should be shipped and distributed together.
- *If more than one type of DTP is being stored, DTP that is not approved for reconstitution should not be stored where there is any chance of confusion with the DTP that is approved for reconstitution.*

5.3 Monitoring vaccine use and wastage

Monitoring vaccine use and wastage becomes increasingly important as the costs of the vaccine rise. Stock monitoring increases ordering accuracy and reduces wastage by providing reliable data for estimating the number and size of vials to be ordered. It also serves as a tool for improving the practices of health centres when wastage rates are found to be unacceptably high.

- The data needed to determine Hib wastage in a given time period are: 1) the number of vials present at the beginning of the period, the number received, and the number remaining at the end; and 2) the number of immunizations given (or doses used).
- Using wastage data for other vaccines to estimate Hib wastage is not necessarily helpful: in one study, wastage estimates for different vaccines ranged from 7% to 79%!

If routine wastage reporting for all vaccines is not possible, consider:

- Reporting Hib wastage for a short period, e.g. one year, to establish a history and then discontinue the reporting process.
- Selecting several vaccines among all vaccines in the programme to serve as wastage indicators, if it can be established that wastage for these vaccines can accurately measure wastage of others not being measured.

5.4 Estimating injection equipment requirements

The injection equipment for Hib vaccine is the same type as that for DTP:	
0.5 ml syringe	
25 mm, 23 gauge needle	

For reconstitution:	
Multi-dose:	5.0 ml syringe 18 gauge needle
Single-dose:	0.5 ml syringe 25 mm, 23 gauge needle

Additional needs for the following must also be estimated:

- Storage space for the syringes and needles
- Sterilization equipment for reusable syringes and needles
- Disposal boxes ("sharps boxes") for disposing of used syringes and needles
- Incinerator capacity for destroying used syringes and needles

5.5 Maintaining injection safety

Unsafe injection practices are widespread and need to be addressed with respect to all injections, including Hib. The introduction of a new vaccine like Hib is a good opportunity to re-enforce safety lessons. **All injection equipment must be sterile each time a patient is given an injection.**

5.6 Monitoring coverage and adverse events

Coverage. Monitoring of Hib vaccine coverage should be incorporated into routine coverage monitoring systems at the same time as the vaccine is introduced.

At minimum, monitoring should include the proportion of children who complete the Hib primary series of three doses by 12 months of age. It may also include:

- The proportion of the target population receiving 1, 2, and 3 doses of Hib vaccine.
- The number of fully immunized children (FIC), which will now be defined as including 3 doses of Hib, as well as the traditional EPI vaccines.
- The drop-out rate

In the first year, health workers should look for impact of the new vaccine on coverage of other vaccines and on the numbers of fully immunized children.

Adverse events. Freeze-dried vaccines (i.e. measles and BCG) have been associated with some adverse events following immunization (AEFI). In many cases, the evidence suggests that the wrong diluent was used or that reconstituted vaccine was bacterially contaminated due to mishandling. This emphasizes the importance of monitoring adverse events following immunization with reconstituted Hib vaccine and assuring prompt investigation and corrective action.

5.7 Hib disease surveillance

Disease surveillance strategies may be used to determine the burden of Hib disease before a decision is made to include Hib vaccine in the routine immunization schedule.

After the introduction of the vaccine, hospitals and laboratories should be the focus of responsibility for case reporting since Hib disease can only be confirmed through laboratory testing. Difficulties in diagnosis of the many types of Hib disease have led to surveillance strategies focusing on meningitis alone, or meningitis and blood stream infection.

See Annex 1 for Hib disease surveillance standards.

5.8 Revision of documents (immunization schedules, children's immunization cards, tally sheets)

Tally sheets and reporting forms, documents for parents, and informational material will be affected by the inclusion of Hib vaccine in an immunization programme. Old immunization schedules must be immediately replaced with schedules that include Hib vaccine.

The best practice is to distribute new materials before Hib vaccine is introduced. Alternatively, health workers may add the Hib data by hand to existing forms and use them as long as they last. However, errors and omissions are more likely to occur if the latter course is chosen.

5.9 Preparation of staff

For the introduction of Hib vaccine, as for any change, managers must determine whose work will be affected and how. Consider the following in assessing the need for Hib training:

- What adjustments will health workers have to make in order to include Hib disease incidence and Hib immunizations in recording and reporting?
- How can health workers communicate effectively with parents and other members of the public about Hib. (See the key messages in Section 5.10 below.)
- If you are introducing lyophilized Hib vaccine, how will you ensure that health workers get supervised practice in reconstituting and administering Hib vaccine?
- If you are using a catch-up strategy, health workers must administer two schedules: the routine schedule for the new birth cohort and the catch-up schedule. What is the best way to help health workers organize patients so the proper immunizations are given?
- If you are using more than one formulation of Hib vaccine, e.g. monovalent Hib for catch-up and combination Hib-DTP for routine, what is the best way to help health workers plan for storage?

Information for health workers is available in Annex 2: Information for health workers – Introduction of Hib vaccine into the routine immunization programme, which addresses:

- Hib disease burden
- Properties of Hib vaccine
- Transport and storage requirements
- Reconstitution and administration
- Immunization schedule
- Documentation

5.10 Hib immunization promotion

Information for the public about the availability and schedule of Hib immunization should include:

- Hib disease and Hib vaccine safety and effectiveness.
- The target population and how it was chosen. Explanation of why older children are not being immunized with Hib vaccine.
- The vaccine's limitations, i.e. it does not prevent all forms of pneumonia and meningitis.

References

Generic protocol for population-based surveillance of Haemophilus influenzae type B. WHO/VRD/GEN/95.05

Information for health workers – Introduction of Hib vaccine into the routine immunization programme – Annex 2.

Information for parents – Introduction of Hib vaccine into your child's immunization programme – Annex 3.

Product Information Sheets Edition 2000. WHO/V&B/00.13.

Safety of injections – WHO-UNICEF-UNFPA joint statement on the use of auto-disable syringes in immunizations services. WHO/V&B/99.25.

Surveillance of adverse events following immunization: Field guide for managers of immunization programmes. WHO/EPI/TRAM/93.02 Rev.1.

The WHO Position Paper on Haemophilus influenzae type b conjugate vaccines. *Weekly Epidemiological Record*, 1998. 73:64-71.

Vaccine Vial Monitor and Opened Vial Policy: Questions and Answers. WHO/EPI/LHIS/96.01.

WHO Policy Statement: The use of opened multi-dose vials of vaccine in subsequent immunization sessions. WHO/V&B/00.09.

Annex 1:

Recommendations for surveillance of *Haemophilus influenzae* type b disease¹

***Haemophilus influenzae* type b (Hib) disease**

Rationale for surveillance

Hib is the most common cause of bacterial meningitis in children, and one of the two most common causes of severe bacterial pneumonia. Pneumonia is the largest single remaining infectious disease killer of young children in the developing world. Hib may also cause other diseases, including arthritis, skin infection, and epiglottitis. Surveillance data are critical for clarifying the burden of disease and evaluating the impact of immunization programmes. Although in many countries Hib pneumonia is more common than the other types of infection, diagnosis of Hib pneumonia is extremely difficult. Routine surveillance should focus on meningitis and other Hib infections diagnosed with microbiologic tests on cerebrospinal fluid (CSF), blood, and other body fluids (such as pleural fluid) that usually do not contain bacteria. Such infections are often called “invasive Hib disease”. The most basic surveillance system should focus on meningitis alone, which is the focus of this set of recommendations. Countries may also wish to report potential cases of bacterial meningitis, both as a performance indicator for Hib detection, and to clarify the burden of meningitis attributable to all bacteria.

Recommended case definition

Clinical description

Bacterial meningitis is characterized by acute onset of fever, headache and stiff neck. Meningitis is not specific for Hib disease, and Hib disease cannot be diagnosed on clinical grounds.

Laboratory criteria for diagnosis

Culture method: isolation of Hib from a normally sterile clinical specimen, such as cerebrospinal fluid (CSF) or blood (i.e. culture of Hib from a non-sterile site, such as the throat, does not define Hib disease, since the bacteria can grow in these other areas and not cause disease).

Antigen detection methods: identification of Hib antigen in normally sterile fluids (i.e. CSF or blood) by antigen detection methods such as latex agglutination or counter immunoelectrophoresis (CIE).

¹ Based on *WHO-recommended standards for surveillance of selected vaccine-preventable diseases* (WHO/EPI/GEN/98.01 Rev.1).

Haemophilus influenzae type b (Hib) disease (continued)

Case classification

Potential: Bacterial meningitis case: a child with a clinical syndrome consistent with bacterial meningitis

Probable: Not applicable

Confirmed: A case that is laboratory confirmed by growing or identifying Hib in the CSF or blood

Note: Any person with Hib isolated from CSF or blood may be reported as a confirmed case, regardless of whether their clinical syndrome was meningitis.

Recommended types of surveillance

- Routine monthly reporting of aggregate data of confirmed cases is recommended from peripheral level to intermediate and central levels
- All potential cases and case-based data should be reported if laboratory performance indicators are to be monitored (see Note)

Note: Since laboratory confirmation is required for all cases, the extent of surveillance will vary depending on the capabilities of individual countries. Surveillance does not need to be national in scope to fulfil goals as noted in “Principles” section below. It is more important to have a well-functioning system in some areas than to have a national system that functions poorly.

Recommended minimum data elements

Aggregated data for reporting

- Number of cases
- Number of 3rd doses of Hib vaccine (Hib3) administered to infants

Case-based data for reporting and investigation

- Unique identifier
- Geographical area (e.g. district and province) names
- Date of birth
- Date of onset
- Specimen type, if specimen collected:
2=CSF; 1=blood; 3=both; 4=other
- Culture result, if done:
1=positive; 2=negative; 3=pending; 4=not done
- Antigen detection result, if done:
1=positive; 2=negative; 3=pending; 4=not done
- CSF white cell count/ml, if done
- Outcome:
1=alive; 2=dead; 9=unknown
- Number of Hib doses received:
9=unknown
- Final classification:
1=potential; 2=confirmed

Haemophilus influenzae type b (Hib) disease (continued)

Recommended data analyses, presentation, reports

Aggregated data

- Incidence rate by year and geographic area
- Hib3 coverage by year and geographic area
- Completeness and timeliness of reporting

Case-based data: Same as aggregate plus:

- Age-specific incidence rate
- Case fatality rate
- Cases by immunization status
- **Performance indicators of surveillance quality**

	Target
– Percent of all potential bacterial meningitis cases for which CSF/blood was obtained for evaluation	³ 90%
– Percent of potential bacterial meningitis cases in which a bacterial pathogen was identified from CSF or blood:	
– Among CSF with 10 or more white blood cells/ml	³ 10%
– Among CSF with 100 or more white blood cells/ml	³ 25%

Note: Although persons with bacterial meningitis have a wide range of CSF white blood cell counts, the proportion of potential bacterial meningitis cases with identifiable bacterial causes increases with increasing CSF cell counts. For evaluation of performance, programme personnel may wish to determine proportion of potential bacterial meningitis cases in which bacterial causes have been identified in one or both of the above categories. Results below the target levels suggest some cases of bacterial meningitis are not being identified, and that review of laboratory and clinical practices should be performed.

Principle uses of data for decision-making

- To determine incidence of Hib meningitis and invasive disease for estimation of Hib disease burden
- To measure impact of immunization programme and identify areas needing additional input
- To monitor coverage and take action to correct low coverage areas

Special aspects

Since Hib surveillance requires laboratory confirmation, nationwide surveillance may not be practical in many countries. However, most surveillance goals may be approached with a less comprehensive plan. Surveillance in areas with appropriate clinical and laboratory capacity can provide necessary information on burden and immunization impact. This may be as simple as hospital-based reporting of Hib meningitis cases in one or more hospitals with this capacity. Coverage data should be obtained nationwide. Evaluating the combination of nationwide coverage data, and area-specific disease data can provide necessary information for making immunization programme decisions. Additional guidance on surveillance methodology can be obtained in WHO publication WHO/VRD/GEN/95.05.

Annex 2:

Information for health workers — Introduction of Hib vaccine into the routine immunization programme

Hib disease

What is Hib? What diseases does it cause?

Hib is the abbreviation for *Haemophilus influenzae type b*, a bacterium that causes severe infections, including:

- Bacterial meningitis – inflammation of the membranes that cover and protect the spinal cord and brain.
- Pneumonia – inflammation of the lungs. Also called acute respiratory infection (ARI) or acute lower respiratory infection (ALRI) .
- Epiglottitis – inflammation of the area around the vocal cords and obstruction of the airway.
- Septicaemia – presence of pathogenic bacteria in the blood; also called blood poisoning.
- Septic arthritis – inflammation of the joints

Hib also causes osteomyelitis (inflammation of the bones), facial cellulitis (inflammation of tissue under the skin), and pericarditis (inflammation of the membrane around the heart), but these diseases are less common.

Hib disease is not the same as hepatitis B (HepB), which is a viral disease that affects the liver.

Why is Hib disease a public health problem?

Hib disease is a public health problem because:

- It causes serious diseases that can result in hospitalization or death, including:
Pneumonia: This is the major cause of death of children in the developing world. A study in Africa showed that approximately 20% of serious bacterial pneumonia cases were caused by the Hib bacterium.
Bacterial meningitis: Hib is the most common cause of bacterial meningitis in most countries. Up to 40% of children with Hib meningitis in developing countries die and 20% of the survivors have permanent brain damage.
- It is easily spread, although not everyone who has the bacterium becomes sick.

How is it spread?

Hib bacteria are passed from child to child in droplets of saliva expelled when an infected child coughs or sneezes. Hib also spreads among children when they share toys and other things that they have put in their mouths.

Who can get Hib infections? Who is most at risk?

Hib disease most often affects children under five years old; children between four months and 12 months of age are most at risk. By age five most children have developed antibodies against the disease, so serious disease is uncommon in older children and adults.

Do antibiotics work against Hib infections?

Antibiotics are used for treatment of Hib disease, but they are not always effective. Even with antibiotics and the best medical care, 3 to 5% of meningitis patients die. Some strains of Hib are now resistant to antibiotics, making treatment even more difficult.

Hib immunization

How can Hib infections be prevented?

Most Hib infections can only be prevented by Hib vaccine. A small proportion of cases can be averted by giving antibiotics to members of households where children have been infected, but at best, this amounts to only 1 to 2% of cases.

What are the limitations of Hib vaccine?

Hib vaccine protects only against diseases caused by the Hib bacterium. After Hib immunization, a child may get pneumonia, meningitis, or flu caused by other bacteria and viruses.

Who should be immunized with Hib vaccine?

Generally, all children should receive Hib vaccine in infancy, after six weeks of age.

How many doses are needed? When should they be given?

Hib immunization schedules differ from country to country depending on the type of Hib vaccine used and the immunization schedule for other vaccines.

In most places:

- Three doses are given.
- The first dose is given only after a child is 6 weeks old.
- The interval between doses is not less than 1 month.

Ask your supervisor for the Hib immunization schedule in your area.
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What is the size of a dose?

The size of each dose is 0.5ml.

Where is it given?

Hib vaccine is given by intramuscular injection in the anterolateral aspect of the thigh (infants) or deltoid muscle (older children).

It can be given at the same time as diphtheria, tetanus, pertussis (DTP), polio (OPV), and hepatitis B (HepB) vaccines without ill effect. If Hib vaccine is given on the same day as another vaccine, it should not be injected in the same limb.

Ask your supervisor what the recommended injection site is for each vaccine.

What are the side effects of Hib vaccine?

Hib vaccine has not been associated with serious side effects. However, redness, swelling, and pain may occur where the injection was given. These usually start within one day after the immunization and last from one to three days. Less commonly, children may develop fever for a short time after immunization.

Is there any reason why a child should not be given Hib vaccine?

Although serious side effects have not been reported, a child who has had a severe reaction to Hib vaccine should not be given another dose.

Immunization may be postponed if a child has a fever.

Handling Hib vaccine

What types of Hib vaccine are available?

Hib vaccines are available in two formulations (liquid or freeze-dried), each of which is available as monovalent or combination preparations. Many countries give Hib as a combined vaccine with DTP, or DTP and hepatitis B.

Ask your supervisor what type of Hib vaccine you will be using and what size of vials will be available.

How should Hib vaccine be stored?

Hib vaccine should be stored between 2°C and 8°C. If liquid Hib vaccine is frozen, discard it.

How does the multi-dose vial policy apply?

Ask your supervisor how the multi-dose vial policy applies.

Other information

What injection equipment is needed?

The same size needle and syringe that is required for injecting DTP and Hib vaccines:

25 mm, 23 gauge needles

0.5 ml syringes

If you are using freeze-dried Hib vaccine, you will need 18 gauge mixing needles and 5 ml syringes.

Used needles and syringes must be sterilized or disposed of in accordance with national policy.

What records are needed to monitor Hib vaccine use, wastage, and immunization coverage?

Monitoring use, wastage, and coverage gives you information about how effective you are in meeting immunization targets and how efficient you are in using vaccine.

Ask your supervisor how to monitor and report vaccine use, wastage, and coverage.

How should Hib disease incidence be monitored?

Your health facility may have participated in Hib disease surveillance before the introduction of Hib vaccine to identify the burden of Hib disease in your area. Now, your facility may be monitoring Hib incidence to determine how effective immunization has been. Your role is important.

Ask your supervisor whether you should be reporting cases and how to do it.

Annex 3:

Information for parents — Introduction of Hib vaccine into your child's immunization programme

Hib disease

What is Hib? What diseases does it cause?

Hib is the abbreviation for *Haemophilus influenzae* type b, a germ that causes severe infections, including:

- Bacterial meningitis – an infection of the protective coverings of the brain and spinal cord
- Pneumonia – an infection of the lungs
- Epiglottitis – an infection of the throat
- Septicaemia – an infection of the blood; also called blood poisoning
- Septic arthritis – an infection of the joints

Hib also can cause problems with the bones, the heart, and the soft tissue under the skin, but these diseases are less common.

Hib disease is NOT the same as hepatitis B. The vaccine against hepatitis B is a different vaccine called hepatitis b or HepB vaccine.

Why is Hib disease a problem?

Hib disease is a problem because:

- It often results in serious illness and/or death. For children who survive the disease, Hib meningitis can lead to permanent brain damage.
- It affects infants and children.
- It is easily spread.

Who can get Hib infections? Who is most at risk?

Hib disease is most common in children under five years of age; children between four and 12 months are most at risk.

Infants who are breast-feeding receive some protection from Hib disease from their mothers. The disease is rare in older children and adults.

Close contact with other children increases the risk of Hib infection.

How is it spread?

Hib germs are passed from child to child in droplets of moisture that come out of an infected child's mouth when he or she coughs or sneezes. Hib is also spread through shared toys and other things that children put in their mouths.

How can Hib be prevented?

Hib vaccine will prevent all diseases caused by Hib bacteria in most children.

Hib vaccine does not protect against diseases caused by other germs. Thus, after Hib immunization, a child may still get other types of pneumonia and meningitis or virus infections, such as flu.

Who should be immunized with Hib vaccine?

All infants older than six weeks of age should have Hib vaccine.

Do older children need Hib vaccine?

Children over four or five years of age have usually developed a natural protection against the disease, so older children do not normally need Hib vaccine.

How many doses are needed? When should they be given?

Hib immunization schedules differ from country to country. Usually:

- Three doses are given.
- The first dose is given only after a child is 6 weeks old.
- The interval between doses is not less than 1 month.

Ask your health care provider for the schedule in your area.

How is Hib vaccine given?

Hib vaccine is given by injection in the anterolateral aspect of the thigh (infants) or deltoid muscle (older children). It can safely be given at the same time as diphtheria, tetanus, pertussis (DTP), polio, and hepatitis B vaccines.

What are the side effects?

Hib vaccine does not cause any serious side effects. However, redness, swelling, and pain may occur where the injection was given. These usually start within one day after the immunization and last from one to three days. Less commonly, children may develop fever for a short time after immunization.

Is there any reason why a child should not be given Hib vaccine?

Although serious side effects have not been reported, a child who has had a severe reaction to Hib vaccine should not be given another dose.